BRIEF SUMMARY OF THE INVENTION

The present application identifies, for the first time, a number of proteins and DNA molecules involved in regulation of angiogenesis, *e.g.*, angiogenesis regulatory proteins and DNA molecules. The invention further relates to methods for identifying and using agents, including small organic molecules, antibodies, peptides, cyclic peptides, nucleic acids, antisense nucleic acids, RNAi, and ribozymes, that modulate angiogenesis via modulation of angiogenesis regulatory proteins and DNA molecules; as well as to the use of expression profiles and compositions in diagnosis and therapy of diseases related to insufficient or increased angiogenesis.

In one aspect, the present invention provides a method for identifying a compound that modulates angiogenesis, the method comprising the steps of:

(i) contacting the compound with an angiogenesis regulatory nucleic acid, or an angiogenesis regulatory polypeptide or a fragment thereof encoded by a nucleic acid, wherein the nucleic acid hybridizes under stringent conditions to a second nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:32, SEQ ID NO:43, SEQ ID NO:57, SEQ ID NO:63, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:76, SEQ ID NO:81, SEQ ID NO:86, SEQ ID NO:89, SEQ ID NO:120, SEQ ID NO:128, SEQ ID NO:139, SEQ ID NO:153, SEQ ID NO:163, SEQ ID NO:165, SEQ ID NO:169, SEQ ID NO:171, SEQ ID NO:173, SEQ ID NO:175, SEQ ID NO:183, SEQ ID NO:202, SEQ ID NO:210, SEQ ID NO:218, SEQ ID NO:227, SEQ ID NO:232, SEQ ID NO:248, SEQ ID NO:274, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:297, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:320, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:340, SEQ ID NO:351, SEQ ID NO:365, SEQ ID NO:377, SEQ ID NO:384, SEQ ID NO:406, SEQ ID NO:408, SEQ ID NO:419, SEQ ID NO:421, SEQ ID NO:428, SEQ ID NO:437, SEQ ID NO:439, SEQ ID NO:445, SEQ ID NO:456, SEQ ID NO:462, SEQ ID NO:481, SEQ ID NO:484, SEQ ID NO:493, SEQ ID NO:496, SEQ ID NO:498, SEQ ID NO:519, SEQ ID NO:521, and SEQ ID NO:523; and (ii) determining the functional effect of the compound upon the nucleic acid or polypeptide.

In one embodiment, the functional effect is determined in vitro. In another embodiment, the functional effect is a physical effect. In another embodiment, the functional effect is determined by measuring ligand or substrate binding to the polypeptide. In another embodiment, the functional effect is a chemical effect. In another embodiment, the functional effect is determined by measuring an enzymatic activity.

In one embodiment, the polypeptide is expressed in a eukaryotic host cell. In a further embodiment, the functional effect is a physical effect. In another embodiment, the functional effect is determined by measuring ligand or substrate binding to the polypeptide. In a further embodiment, the functional effect is a chemical or phenotypic effect. In another embodiment, the functional effect is determined by measuring an enzymatic activity. In another embodiment, the host cell is an endothelial cell. In a further embodiment, the functional effect is determined by measuring $\alpha v\beta 3$ expression or haptotaxis, or chemotaxis, or co-culture tube formation.

In one embodiment, modulation is inhibition of angiogenesis.

In one embodiment, the polypeptide is recombinant. In another embodiment, the nucleic acid comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:32, SEQ ID NO:43, SEQ ID NO:57, SEQ ID NO:63, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:76, SEQ ID NO:81, SEQ ID NO:86, SEQ ID NO:89, SEQ ID NO:120, SEQ ID NO:128, SEQ ID NO:139, SEQ ID NO:153, SEQ ID NO:163, SEQ ID NO:165, SEQ ID NO:169, SEQ ID NO:171, SEQ ID NO:173, SEQ ID NO:175, SEQ ID NO:183, SEQ ID NO:202, SEQ ID NO:210, SEQ ID NO:218, SEQ ID NO:227, SEQ ID NO:232, SEQ ID NO:248, SEQ ID NO:274, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:297, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:320, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:340, SEQ ID NO:351, SEQ ID NO:365, SEQ ID NO:377, SEQ ID NO:384, SEQ ID NO:406, SEQ ID NO:408, SEQ ID NO:419, SEQ ID NO:421, SEQ ID NO:428, SEQ ID NO:437, SEQ ID NO:439, SEQ ID NO:445, SEQ ID NO:456, SEQ ID NO:462, SEQ ID NO:481, SEQ ID NO:484, SEQ ID NO:493, SEQ ID NO:496, SEQ ID NO:498, SEQ ID NO:519, SEQ ID NO:521, and SEQ ID NO:523.

In another embodiment, the polypeptide comprises a sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:33, SEQ ID NO:44, SEQ ID NO:58, SEQ ID NO:64, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:77, SEQ ID NO:82, SEQ ID NO:87, SEQ ID NO:90, SEQ ID NO:121, SEQ ID NO:129, SEQ ID NO:140, SEQ ID NO:154, SEQ ID NO:164, SEQ ID NO:170, SEQ ID NO:172, SEQ ID NO:174, SEQ ID NO:176, SEQ ID NO:184, SEQ ID NO:203, SEQ ID NO:287, SEQ ID NO:298, SEQ ID NO:309, SEQ ID NO:319, SEQ ID NO:325, SEQ ID NO:331, SEQ ID NO:341, SEQ ID NO:352, SEQ ID NO:366, SEQ ID NO:378, SEQ ID NO:385, SEQ ID NO:407, SEQ ID NO:409, SEQ ID NO:420, SEQ ID NO:429, SEQ ID NO:438, SEQ ID NO:440, SEQ ID NO:446, SEQ ID

NO:457, SEQ ID NO:463, SEQ ID NO:482, SEQ ID NO:485, SEQ ID NO:494, SEQ ID NO:497, SEQ ID NO:499, SEQ ID NO:520, SEQ ID NO:522, and SEQ ID NO:524.

In one embodiment, the compound is an antibody, an antisense molecule, a small organic molecule, or a peptide.

In another aspect, the present invention provides a method for identifying a compound that modulates angiogenesis, the method comprising the steps of (i) contacting the compound with a nucleic acid, or a polypeptide or a fragment thereof encoded by a nucleic acid, wherein the nucleic acid hybridizes under stringent conditions to a second nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:32, SEQ ID NO:43, SEQ ID NO:57, SEQ ID NO:63, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:76, SEQ ID NO:81, SEQ ID NO:86, SEQ ID NO:89, SEQ ID NO:120, SEQ ID NO:128, SEQ ID NO:139, SEQ ID NO:153, SEQ ID NO:163, SEQ ID NO:165, SEQ ID NO:169, SEQ ID NO:171, SEQ ID NO:173, SEQ ID NO:175, SEQ ID NO:183, SEQ ID NO:202, SEQ ID NO:210, SEQ ID NO:218, SEQ ID NO:227, SEQ ID NO:232, SEQ ID NO:248, SEQ ID NO:274, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:297, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:320, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:340, SEQ ID NO:351, SEQ ID NO:365, SEQ ID NO:377, SEQ ID NO:384, SEQ ID NO:406, SEQ ID NO:408, SEQ ID NO:419, SEQ ID NO:421, SEQ ID NO:428, SEQ ID NO:437, SEQ ID NO:439, SEQ ID NO:445, SEQ ID NO:456, SEQ ID NO:462, SEQ ID NO:481, SEQ ID NO:484, SEQ ID NO:493, SEQ ID NO:496, SEQ ID NO:498, SEQ ID NO:519, SEQ ID NO:521, and SEQ ID NO:523; (ii) determining the functional effect of the compound upon the nucleic acid or polypeptide; and (iii) expressing the nucleic acid or polypeptide in a cell, contacting the nucleic acid or polypeptide with the compound, and determining the phenotypic or chemical effect upon the cell.

In another aspect, the present invention provides a method of modulating angiogenesis in a subject, the method comprising the step of administering to the subject a therapeutically effective amount of a compound identified as a modulator of angiogenesis using the methods described herein. In one embodiment, the subject is a human. In a further embodiment, the compound is an antibody, an antisense molecule, a small organic molecule, a peptide, or an RNAi molecule. In another embodiment, the compound inhibits angiogenesis.

In another aspect, the present invention provides a method of modulating angiogenesis in a subject, the method comprising the step of administering to the subject a

therapeutically effective amount of a polypeptide, the polypeptide encoded by a nucleic acid that hybridizes under stringent conditions to a second nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:76, SEQ ID NO:81, SEQ ID NO:86, SEQ ID NO:89, SEQ ID NO:120, SEQ ID NO:128, SEQ ID NO:165, SEQ ID NO:183, SEQ ID NO:202, SEQ ID NO:218, SEQ ID NO:232, SEQ ID NO:274, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:297, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:320, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:340, SEQ ID NO:377, SEQ ID NO:384, SEQ ID NO:406, SEQ ID NO:408, SEQ ID NO:439, SEQ ID NO:445, SEQ ID NO:456, SEQ ID NO:481, SEQ ID NO:484, SEQ ID NO:493, SEQ ID NO:496, and SEQ ID NO:498.

In another aspect, the present invention provides a method of modulating angiogenesis in a subject, the method comprising the step of administering to the subject a therapeutically effective amount of a nucleic acid that hybridizes under stringent conditions to a second nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:32, SEQ ID NO:43, SEQ ID NO:57, SEQ ID NO:63, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:76, SEQ ID NO:81, SEQ ID NO:86, SEQ ID NO:89, SEQ ID NO:120, SEQ ID NO:128, SEQ ID NO:139, SEQ ID NO:153, SEQ ID NO:163, SEQ ID NO:165, SEQ ID NO:169, SEQ ID NO:171, SEQ ID NO:173, SEQ ID NO:175, SEQ ID NO:183, SEQ ID NO:202, SEQ ID NO:210, SEQ ID NO:218, SEQ ID NO:227, SEQ ID NO:232, SEQ ID NO:248, SEQ ID NO:274, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:297, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:320, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:340, SEQ ID NO:351, SEQ ID NO:365, SEQ ID NO:377, SEQ ID NO:384, SEQ ID NO:406, SEQ ID NO:408, SEQ ID NO:419, SEQ ID NO:421, SEQ ID NO:428, SEQ ID NO:437, SEQ ID NO:439, SEQ ID NO:445, SEQ ID NO:456, SEQ ID NO:462, SEQ ID NO:481, SEQ ID NO:484, SEQ ID NO:493, SEQ ID NO:496, SEQ ID NO:498, SEQ ID NO:519, SEQ ID NO:521, and SEQ ID NO:523.

In another aspect, the present invention provides the nucleic acid sequences of SEQ ID NO:165, SEQ ID NO:202, SEQ ID NO:210, SEQ ID NO:218, SEQ ID NO:227, SEQ ID NO:232, SEQ ID NO:248, SEQ ID NO:274, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:297, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:320, SEQ ID NO:323, SEQ ID NO:324, ~~SEQ ID:329~~ SEQ ID NO:329, and ~~SEQ ID:330~~ SEQ ID NO:330.

In another aspect, the present invention provides the amino acid sequences of SEQ ID NO:287, SEQ ID NO:298, SEQ ID NO:309, SEQ ID NO:319, SEQ ID NO:325, and SEQ ID NO:331.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 provides a schematic diagram of an assay for modulators of angiogenesis.

Figure 2 provides results of an experiment demonstrating the effect of a plakoglobin-GFP fusion protein expression on levels of the cell surface marker $\alpha v\beta 3$. Plakoglobin is an exemplar angiogenesis regulatory protein. Human umbilical vein endothelial (HUVEC) cells were transfected with a vector expressing the plakoglobin-GFP fusion protein ($(GGS)_2$ = SEQ ID NO:525) or a control vector, expressing GFP only. Cells were incubated with APC-labeled antibodies directed against the cell surface marker $\alpha v\beta 3$. The X-axis depicts cell number and the Y-axis depicts the amount of $\alpha v\beta 3$-APC antibody derived fluorescence. Cells transfected with the plakoglobin-GFP fusion protein construct exhibit lower $\alpha v\beta 3$ expression levels than control cells.

Figure 3 also provides results of an experiment demonstrating the effect of a plakoglobin-GFP fusion protein (*i.e.*, GFP-ΔN-plakoglobin) expression on levels of the cell surface marker $\alpha v\beta 3$. The figure also depicts the presence of armadillo repeats in the functional screen hit, GFP-ΔN-plakoglobin.

Figure 4 demonstrates that GFP-ΔN-Plako expression downregulates vitronectin receptors ($\alpha v\beta 3$ and $\alpha v\beta 5$) but not the fibronectin receptor ($\alpha 5\beta 1$).

Figure 5 demonstrates that expression of GFP-ΔN-Plakoglobin downregulates endogenous catenin levels, as well as expression of endogenous plakoglobin and VE-cadherin.

Figure 6 demonstrates that GFP-ΔN-Plakoglobin expression upregulates surface levels of the laminin receptor, $\alpha 6\beta 4$.

Figure 7 provides provides results of an experiment demonstrating the effect of a HoxB2-GFP fusion protein expression (*i.e.*, ΔN-HoxB2) on levels of the cell surface marker $\alpha v\beta 3$. Cells transfected with the ΔN-HoxB2-GFP fusion protein construct exhibit lower $\alpha v\beta 3$ expression levels than control cells. The figure also provides the structure of the functional screen hit, demonstrating that the homeodomain is present in ΔN-HoxB2.

Figure 8 demonstrates that ΔN-HoxB2 downregulates both αv and $\beta 3$ integrin subunit surface expression, as well as $\alpha v\beta 5$ surface expression.

Figure 9 demonstrates that ΔN-HoxB2 Inhibits Proliferation in HUVECs, a primary cell line.

Figure 10 demonstrates that full length HoxB2 phenocopies ΔN-HoxB2 in the downregulation of $\alpha v\beta 3$.

Figure 11 provides provides results of an experiment demonstrating the effect of a SUSP-1 GFP fusion protein expression (*i.e.*, GFP-SUSP-1) on levels of the cell surface marker $\alpha v\beta 3$. Cells transfected with the GFP-SUSP-1 fusion protein construct exhibit lower $\alpha v\beta 3$ expression levels than control cells. The figure also provides the structure of the functional screen hit, demonstrating that GFP-SUSP-1 is an N-terminal fusion in the sense orientation and that a cDNA insert is present before the wild-type start codon.

Figure 12 demonstrates that the GFP-SUSP-1 screening hit does not affect proliferation when expressed in HUVEC (human umbilical vein endothelial cells), PASMC (pulmonary artery smooth muscle cells), and NHDF (normal human dermal fibroblasts).

Figure 13 provides expression analysis of SUSP-1 mRNA in a variety of cell lines.

Figure 14 demonstrates that SUSP-1 siRNAs inhibit SUSP-1 mRNA expression.

Figure 15 provides a new sequence determination for a nucleic acid encoding an ABC transporter protein. (SEQ ID NO:2)

Figure 16 provides a new sequence determination for a nucleic acid encoding an HSPA5 protein. (SEQ ID NO:127)

Figure 17 provides a new sequence determination for a nucleic acid encoding a protein disulfide isomerase. (SEQ ID NO:165)

Figure 18 provides a new sequence determination for a nucleic acid encoding a novel protein from human chromosome 1. (SEQ ID NO:210)

Figure 19 provides a new sequence determination for a nucleic acid encoding a novel protein from human chromosome 3. (SEQ ID NO:218)

Figure 20 provides a new sequence determination for a nucleic acid encoding a novel protein from human chromosome 17. (SEQ ID NO:227).

Figure 21 provides a new sequence determination for a nucleic acid encoding a novel protein from human chromosome 8. (SEQ ID NO:232)

Figure 22 provides a new sequence determination for a nucleic acid encoding a novel protein from human chromosome 9. (SEQ ID NO:248)

Figure 23 provides a new sequence determination for a nucleic acid encoding a 1/226 protein$_\lambda$. (SEQ ID NO:274)

Figure 24 provides a new sequence determination for a nucleic acid encoding an FLJ10688 protein$_\lambda$. (SEQ ID NO:285)

Figure 25 provides a new sequence determination for a nucleic acid encoding a KIAA1583 protein$_\lambda$. (SEQ ID NO:307)

Figure 26 provides a new sequence determination for a nucleic acid encoding a KIAA1814 protein$_\lambda$. (SEQ ID NO:317)

Figure 27 provides a new sequence determination for a nucleic acid encoding a novel protein from human chromosome 4$_\lambda$. (SEQ ID NO:320)

Figure 28 provides a new sequence determination for a nucleic acid encoding a peroxidasin/melanoma antigen related protein$_\lambda$. (SEQ ID NO:323)

Figure 29 provides a new sequence determination for a nucleic acid encoding a WD40/SOCS box protein$_\lambda$. (SEQ ID NO:329)

Figure 30 provides provides results of an experiment demonstrating the effect of a Δ5FADS antisense screening hit (*i.e.*, GFP-Δ5FADS or D5ADS) on levels of the cell surface marker $\alpha v\beta 3$. Cells transfected with the GFP- Δ5FADS antisense construct exhibit lower $\alpha v\beta 3$ expression levels than control cells. The figure also provides the structure of the functional screen hit, demonstrating that GFP- Δ5FADS is in the antisense orientation and that a the anti sense portion of the Δ5FADS nucleic acid is about 300 base pairs long.

Figure 31 demonstrates that the GFP-D5FADS antisense screening hit does not affect cell proliferation.

Figure 32 demonstrates that Δ5FADS siRNAs inhibit Δ5FADS mRNA expression.

Figure 33 demonstrates that Δ5FADS siRNAs inhibit haptotaxis.

Figure 34 demonstrates that Δ5FADS siRNAs inhibit SDF-1 induced chemotaxis in Jurkat cells.

Figure 35 demonstrates that Δ6FADS is a functional screening hit. The figure shows that Δ6FADS transcript is spliced to the KIAA1583 functional screen hit.

Figure 36 demonstrates tha Δ6FADS mRNA levels are straongly reduced in cells that express the antisense KIAA1583 functional screen hit.

Figure 37 that Δ6FADS siRNAs inhibit Δ6FADS mRNA expression and also reduce $\alpha v\beta 3$ surface expression.

DETAILED DESCRIPTION OF THE INVENTION

Introduction

Using a functional assay, angiogenesis regulatory proteins and nucleic acids have been identified and cloned from a green fluorescent protein (GFP) fusion library. Primary endothelial cells were transduced with retroviral cDNA/GFP fusion libraries. Transduced cells were selected and assayed for alterations consistent with inhibition of angiogenesis, e.g. downregulation of cell surface expression of $\alpha v\beta 3$ or downregulation of haptotaxis.

Using the screen described above, fifty-two proteins and/or DNA molecules were shown for the first time to regulate angiogenesis. Thirty-four of the proteins and/or DNA molecules are known, while fifteen of the proteins and/or DNA molecules are completely novel. However, this is the first demonstration of a function in regulation of angiogenesis for these molecules.

The ABC transporter is involved in peroxisome biogenesis. Relevant sequence data for the protein, nucleic acids encoding the ABC transporter, and related sequences include the nucleic acid accession number NM_000033, SEQ ID NO:3; protein accession number NP_000024, SEQ ID NO:4; a new sequence determination, SEQ ID NO:2; and the functional screen hit, SEQ ID NO:1. The protein has an ATP-binding domain. The gene encoding the ABC transporter is linked to a genetic disease, adrenoleukodystrophy (Mosser *et al.*, *Nature* 361:682-3 (1993)). An antisense version of the ABC transporter gene, *e.g.*, SEQ ID NO:1, was identified as a functional hit in the screen for modulators of angiogenesis.

PCB1, a poly (rC) binding protein functions as a translational co-activator and also binds 3' UTRs of RNA, most likely through KH domains, thereby regulating RNA stability. Relevant sequence data for the protein, nucleic acids encoding PCB1, and related sequences include the nucleic acid accession number NM_006196, SEQ ID NO:32; protein accession number NP_006187, SEQ ID NO:33; and the functional screen hit, SEQ ID NO:5-31. An antisense version of the gene encoding PCB1 was identified as a functional hit in the screen for modulators of angiogenesis.

SLC1A5, an amino acid transporter, has ten transmembrane spanning segments. Relevant sequence data for the protein, nucleic acids encoding ~~PCB1~~ SLC1A5, and related sequences include the nucleic acid accession number NM_005628, SEQ ID NO:43; protein accession number NP_005619, SEQ ID NO:44; and the functional screen hit, SEQ ID

NO:34-42. An antisense version of the gene encoding SLC1A5 was identified as a functional hit in the screen for modulators of angiogenesis.

Chromobox homolog 6 is involved in chromatin regulation. Relevant sequence data for the protein, nucleic acids encoding chromobox homolog 6, and related sequences include the nucleic acid accession number NM_014292, SEQ ID NO:57; protein accession number NP_055107, SEQ ID NO:58; and the functional screen hit, SEQ ID NO:~~44~~45-56. An antisense version of chromobox homolog 6 was identified as a functional hit in the screen for modulators of angiogenesis.

Cytochrome C oxidase subunit 1 is encoded by a mitochondrial gene and transfers electrons from cytochrome C to O_2 (Ingman *et al.*, *Nature* 408:708-713 (2000); (Leninger, *Principles of Biochemistry* (1984); Stryer, *Biochemistry* (1995)) Relevant sequence data for the protein, nucleic acids encoding cytochrome C oxidase, and related sequences include the nucleic acid accession number NC_001807, SEQ ID NO:63; protein accession number NP_536845, SEQ ID NO:64; and the functional screen hit, SEQ ID NO:59-62. A sense version of the gene encoding cytochrome C oxidase, encoding a 21 amino acid peptide, was identified as a functional hit in the screen for modulators of angiogenesis.

Δ-5 fatty acid desaturase (FADSD5 or Δ5FADS) introduces double bonds into a fatty acyl chain. The protein is involved in arachadonic acid synthesis and has a fatty acid desaturase domain and a heme-binding domain. Relevant sequence data for the protein, nucleic acids encoding Δ-5 fatty acid desaturase, and related sequences include the nucleic acid accession number NM_013402, SEQ ID NO:68; protein accession number NP_037534, SEQ ID NO:69; and the functional screen hit, SEQ ID NO:65-67. An antisense version of Δ-5 fatty acid desaturase gene was identified as a functional hit in the screen for modulators of angiogenesis.

The dynactin p27 subunit protein was shown to be an angiogenesis regulatory protein. The protein has an RGD domain. Relevant sequence data for the protein, and the nucleic acid encoding dynactin p27 subunit protein, include the nucleic acid accession number NC_006571, SEQ ID NO:70; and protein accession number NP_006562.1, SEQ ID NO:71. An antisense version of the gene encoding dynactin p27 subunit protein was identified as a functional hit in the screen for modulators of angiogenesis.

Elongation factor 1 alpha (EF1α) was shown to be involved in regulation of angiogenesis. Relevant sequence data for the protein, nucleic acids encoding EF1α, and related sequences include the nucleic acid accession number NC_001402, SEQ ID NO:76;

functional screen hit. Relevant sequence data for the protein, nucleic acids encoding HSPA5, and related sequences include the nucleic acid accession number NM_005347, SEQ ID NO:128; protein accession number NP_005338, SEQ ID NO:129; a new sequence determination, SEQ ID NO:127; and the functional screen hit, SEQ ID NO:122-126.

Interferon gamma receptor 1 (~~IFNγ1~~ IFNγR1) is a cytokine receptor that induces antiangiogenic genes. Relevant sequence data for the protein, nucleic acids encoding ~~IFNγ1~~ IFNγR1, and related sequences include the nucleic acid accession number NM_000416, SEQ ID NO:139; protein accession number NP_000407, SEQ ID NO:140; and the functional screen hit, SEQ ID NO:130-138. An antisense version of the IFNγ1 gene was identified as a functional hit in the screen for modulators of angiogenesis.

Importin α4 (karyopherin α3) is a subunit of the nuclear localization signal receptor. Relevant sequence data for the protein, nucleic acids encoding importin α4, and related sequences include the nucleic acid accession number NM_002267, SEQ ID NO:153; protein accession number NP_002258.1, SEQ ID NO:154; and the functional screen hit, SEQ ID NO:141-152. An antisense version of the importin α4 gene was identified as a functional hit in the screen for modulators of angiogenesis.

The lysosomal pepstatin-insensitive protease (CLN2) is encoded by a gene associated with juvenile neuronal ceroid lipofuscinosis disease. Relevant sequence data for the protein, nucleic acids encoding CLN2, and related sequences include the nucleic acid accession number NM_000391, SEQ ID NO:163; protein accession number NP_000382, SEQ ID NO:164; and the functional screen hit, SEQ ID NO:155-162. An antisense version of the CLN2 gene was identified as a functional hit in the screen for modulators of angiogenesis.

A novel protein disulfide isomerase was shown to have a role in angiogenesis. Relevant sequence data for the nucleic acid encoding the novel protein disulfide isomerase, includes SEQ ID NO:165. An antisense version of gene encoding the novel protein disulfide isomerase was identified as a functional hit in the screen for modulators of angiogenesis. The antisense hit encodes a 45 or 32 amino acid peptide that may also be useful as a therapeutic or to modulate angiogenesis.

Microtubule-associated protein 4 (MAP4) binds tubulin and may link microtubules to other elements of the cytoskeleton. See *e.g.*, Chapin & Bulinski, *J. Cell. Sci* 98:27-36 (1991); and Chapin *et al.*, *Biochemistry* 34:2289-2301 (1995). Four isoforms of MAP4 are known. Relevant sequence data for the proteins, nucleic acids encoding MAP4 isoforms, and related sequences include the nucleic acid accession numbers NM_002375,

Plasminogen activator inhibitor 1 (SERPINE1 or PAI-1) was identified as an angiogenesis regulatory protein. PAI-1 is a protease inhibitor. Relevant sequence data for the protein, nucleic acids encoding PAI-1, and related sequences include the nucleic acid accession number NM_000602, SEQ ID NO:419; protein accession number NP_000593, SEQ ID NO:420; and the functional screen hit, SEQ ID NO:410-418. The functional screen hit is in the antisense orientation.

Proteosomal subunit Y, an INFγ regulated proteosomal subunit, was identified as an angiogenesis regulatory protein. Relevant sequence data for proteosomal subunit Y includes the functional screen hit, SEQ ID NO:421. The functional screen hit is in the antisense orientation.

Rap2B was identified as an angiogenesis regulatory protein. Rap2B is a member of the RAS family of GTPases. Relevant sequence data for the protein, nucleic acids encoding Rap2B, and related sequences include the nucleic acid accession number XM_003032, SEQ ID NO:428; protein accession number XP_003032, SEQ ID NO:429; and the functional screen hit, SEQ ID NO:422-427. The functional screen hit is in the antisense orientation.

Semaphorin 3F was identified as an angiogenesis regulatory protein. Semaphorin 3F is a ligand for NP2. Relevant sequence data for the protein, nucleic acids encoding semaphorin 3F, and related sequences include the nucleic acid accession number U38276, SEQ ID NO:437; protein accession number AAB18276, SEQ ID NO:438; and the functional screen hit, SEQ ID NO:430-436. The functional screen hit is in the antisense orientation.

SPARC was identified as an angiogenesis regulatory protein. Relevant sequence data for the protein, nucleic acids encoding SPARC, and related sequences include the nucleic acid accession number NM_003118, SEQ ID NO:439; and protein accession number NP_003109, SEQ ID NO:440.

ssDNA binding protein-3 was identified as an angiogenesis regulatory protein. Relevant sequence data for the protein, nucleic acids encoding ssDNA binding protein-1, and related sequences include the nucleic acid accession number NM_018070, SEQ ID NO:445; protein accession number NP_060540, SEQ ID NO:446; and the functional screen hit, SEQ ID NO:441-444. The functional screen hit is in the sense orientation.

Sumo protease (SUSP-1) was identified as an angiogenesis regulatory protein. Relevant sequence data for the protein, nucleic acids encoding SUSP-1, and related sequences include the nucleic acid accession number NM_015571, SEQ ID NO:456; protein

The terms "angiogenesis regulatory protein or nucleic acid" or a nucleic acid encoding "angiogenesis regulatory protein" refer to nucleic acid and polypeptide polymorphic variants, alleles, mutants, and interspecies homologs that: (1) have an amino acid sequence that has greater than about 60% amino acid sequence identity, 65%, 70%, 75%, 80%, 85%, 90%, preferably 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or greater amino acid sequence identity, preferably over a region of over a region of at least about 25, 50, 100, 200, 500, 1000, or more amino acids, to a polypeptide encoded by a nucleic acid of SEQ ID NO:3, SEQ ID NO:32, SEQ ID NO:43, SEQ ID NO:57, SEQ ID NO:63, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:76, SEQ ID NO:81, SEQ ID NO:86, SEQ ID NO:89, SEQ ID NO:120, SEQ ID NO:128, SEQ ID NO:139, SEQ ID NO:153, SEQ ID NO:163, SEQ ID NO:165, SEQ ID NO:169, SEQ ID NO:171, SEQ ID NO:173, SEQ ID NO:175, SEQ ID NO:183, SEQ ID NO:202, SEQ ID NO:210, SEQ ID NO:218, SEQ ID NO:227, SEQ ID NO:232, SEQ ID NO:248, SEQ ID NO:274, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:297, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:320, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:340, SEQ ID NO:351, SEQ ID NO:365, SEQ ID NO:377, SEQ ID NO:384, SEQ ID NO:406, SEQ ID NO:408, SEQ ID NO:419, SEQ ID NO:421, SEQ ID NO:428, SEQ ID NO:437, SEQ ID NO:439, SEQ ID NO:445, SEQ ID NO:456, SEQ ID NO:462, SEQ ID NO:481, SEQ ID NO:484, SEQ ID NO:493, SEQ ID NO:496, SEQ ID NO:498, and SEQ ID NO:519, or an amino acid sequence of SEQ ID NO:4, SEQ ID NO:33, SEQ ID NO:44, SEQ ID NO:58, SEQ ID NO:64, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:77, SEQ ID NO:82, SEQ ID NO:87, SEQ ID NO:90, SEQ ID NO:121, SEQ ID NO:129, SEQ ID NO:140, SEQ ID NO:154, SEQ ID NO:164, SEQ ID NO:170, SEQ ID NO:172, SEQ ID NO:174, SEQ ID NO:176, SEQ ID NO:184, SEQ ID NO:203, SEQ ID NO:287, SEQ ID NO:298, SEQ ID NO:309, SEQ ID NO:319, SEQ ID NO:325, SEQ ID NO:331, SEQ ID NO:341, SEQ ID NO:352, SEQ ID NO:366, SEQ ID NO:378, SEQ ID NO:385, SEQ ID NO:407, SEQ ID NO:409, SEQ ID NO:420, SEQ ID NO:429, SEQ ID NO:438, SEQ ID NO:440, SEQ ID NO:446, SEQ ID NO:457, SEQ ID NO:463, SEQ ID NO:482, SEQ ID NO:485, SEQ ID NO:494, SEQ ID NO:497, SEQ ID NO:499, SEQ ID NO:520, SEQ ID NO:522, and SEQ ID NO:524or other sequences listed herein; (2) specifically bind to antibodies, e.g., polyclonal antibodies, raised against an immunogen comprising an amino acid sequence of SEQ ID NO:4, SEQ ID NO:33, SEQ ID NO:44, SEQ ID NO:58, SEQ ID NO:64, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:77, SEQ ID NO:82, SEQ ID NO:87, SEQ ID NO:90, SEQ ID NO:121, SEQ ID NO:129, SEQ ID NO:140, SEQ ID NO:154, SEQ

ID NO:164, SEQ ID NO:170, SEQ ID NO:172, SEQ ID NO:174, SEQ ID NO:176, SEQ ID NO:184, SEQ ID NO:203, SEQ ID NO:287, SEQ ID NO:298, SEQ ID NO:309, SEQ ID NO:319, SEQ ID NO:325, SEQ ID NO:331, SEQ ID NO:341, SEQ ID NO:352, SEQ ID NO:366, SEQ ID NO:378, SEQ ID NO:385, SEQ ID NO:407, SEQ ID NO:409, SEQ ID NO:420, SEQ ID NO:429, SEQ ID NO:438, SEQ ID NO:440, SEQ ID NO:446, SEQ ID NO:457, SEQ ID NO:463, SEQ ID NO:482, SEQ ID NO:485, SEQ ID NO:494, SEQ ID NO:497, SEQ ID NO:499, SEQ ID NO:520, SEQ ID NO:522, and SEQ ID NO:524, immunogenic fragments thereof, and conservatively modified variants thereof; (3) specifically hybridize under stringent hybridization conditions to a nucleic acid encoding SEQ ID NO:4, SEQ ID NO:33, SEQ ID NO:44, SEQ ID NO:58, SEQ ID NO:64, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:77, SEQ ID NO:82, SEQ ID NO:87, SEQ ID NO:90, SEQ ID NO:121, SEQ ID NO:129, SEQ ID NO:140, SEQ ID NO:154, SEQ ID NO:164, SEQ ID NO:170, SEQ ID NO:172, SEQ ID NO:174, SEQ ID NO:176, SEQ ID NO:184, SEQ ID NO:203, SEQ ID NO:287, SEQ ID NO:298, SEQ ID NO:309, SEQ ID NO:319, SEQ ID NO:325, SEQ ID NO:331, SEQ ID NO:341, SEQ ID NO:352, SEQ ID NO:366, SEQ ID NO:378, SEQ ID NO:385, SEQ ID NO:407, SEQ ID NO:409, SEQ ID NO:420, SEQ ID NO:429, SEQ ID NO:438, SEQ ID NO:440, SEQ ID NO:446, SEQ ID NO:457, SEQ ID NO:463, SEQ ID NO:482, SEQ ID NO:485, SEQ ID NO:494, SEQ ID NO:497, SEQ ID NO:499, SEQ ID NO:520, SEQ ID NO:522, and SEQ ID NO:524, e.g., a nucleic acid sequence of SEQ ID NO:3, SEQ ID NO:32, SEQ ID NO:43, SEQ ID NO:57, SEQ ID NO:63, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:76, SEQ ID NO:81, SEQ ID NO:86, SEQ ID NO:89, SEQ ID NO:120, SEQ ID NO:128, SEQ ID NO:139, SEQ ID NO:153, SEQ ID NO:163, SEQ ID NO:165, SEQ ID NO:169, SEQ ID NO:171, SEQ ID NO:173, SEQ ID NO:175, SEQ ID NO:183, SEQ ID NO:202, SEQ ID NO:210, SEQ ID NO:218, SEQ ID NO:227, SEQ ID NO:232, SEQ ID NO:248, SEQ ID NO:274, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:297, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:320, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:340, SEQ ID NO:351, SEQ ID NO:365, SEQ ID NO:377, SEQ ID NO:384, SEQ ID NO:406, SEQ ID NO:408, SEQ ID NO:419, SEQ ID NO:421, SEQ ID NO:428, SEQ ID NO:437, SEQ ID NO:439, SEQ ID NO:445, SEQ ID NO:456, SEQ ID NO:462, SEQ ID NO:481, SEQ ID NO:484, SEQ ID NO:493, SEQ ID NO:496, SEQ ID NO:498, SEQ ID NO:519, SEQ ID NO:521, and SEQ ID NO:523; or its complement, and conservatively modified variants thereof; (4) have a nucleic acid sequence that has greater than about 95%, preferably greater than about 96%, 97%, 98%, 99%, or higher nucleotide

sequence identity, preferably over a region of at least about 25, 50, 100, 200, 500, 1000, or more nucleotides, to SEQ ID NO:3, SEQ ID NO:32, SEQ ID NO:43, SEQ ID NO:57, SEQ ID NO:63, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:76, SEQ ID NO:81, SEQ ID NO:86, SEQ ID NO:89, SEQ ID NO:120, SEQ ID NO:128, SEQ ID NO:139, SEQ ID NO:153, SEQ ID NO:163, SEQ ID NO:165, SEQ ID NO:169, SEQ ID NO:171, SEQ ID NO:173, SEQ ID NO:175, SEQ ID NO:183, SEQ ID NO:202, SEQ ID NO:210, SEQ ID NO:218, SEQ ID NO:227, SEQ ID NO:232, SEQ ID NO:248, SEQ ID NO:274, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:297, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:320, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:340, SEQ ID NO:351, SEQ ID NO:365, SEQ ID NO:377, SEQ ID NO:384, SEQ ID NO:406, SEQ ID NO:408, SEQ ID NO:419, SEQ ID NO:421, SEQ ID NO:428, SEQ ID NO:437, SEQ ID NO:439, SEQ ID NO:445, SEQ ID NO:456, SEQ ID NO:462, SEQ ID NO:481, SEQ ID NO:484, SEQ ID NO:493, SEQ ID NO:496, SEQ ID NO:498, SEQ ID NO:519, SEQ ID NO:521, and SEQ ID NO:523, or the complement of any of those sequences. A polynucleotide or polypeptide sequence is typically from a mammal including, but not limited to, primate, e.g., human; rodent, e.g., rat, mouse, hamster; cow, pig, horse, sheep, or any mammal. The nucleic acids and proteins of the invention include both naturally occurring or recombinant molecules. When available, accession numbers for the human angiogenesis regulatory proteins and genes are provided.

The phrase "functional effects" in the context of assays for testing compounds that modulate activity of a angiogenesis regulatory proteins includes the determination of a parameter that is indirectly or directly under the influence of a angiogenesis regulatory protein polypeptide, e.g., a chemical or phenotypic effect such as loss-of angiogenesis phenotype represented by a change in expression of a cell surface marker, such as $\alpha v\beta 3$ integrin, or changes in cellular proliferation, especially endothelial cell proliferation; or enzymatic activity, or, e.g., a physical effect such as ligand binding or inhibition of ligand binding. A functional effect therefore includes ligand binding activity, the ability of cells to proliferate, expression in cells undergoing angiogenesis, and other characteristics of angiogenic cells. "Functional effects" include *in vitro*, *in vivo*, and *ex vivo* activities. Angiogenesis assays are described, e.g., in *Angiogenesis Protocols* (Murray, ed., 2001).

By "determining the functional effect" is meant assaying for a compound that increases or decreases a parameter that is indirectly or directly under the influence of a angiogenesis regulatory proteins, e.g., measuring physical and chemical or phenotypic effects. Such functional effects can be measured by any means known to those skilled in the

family, the integrin family, the selectin family, and the like; *see, e.g.*, Pigott & Power, *The Adhesion Molecule Facts Book I* (1993). Similarly, toxins and venoms, viral epitopes, hormones (e.g., opiates, steroids, etc.), intracellular receptors (e.g. which mediate the effects of various small ligands, including steroids, thyroid hormone, retinoids and vitamin D; peptides), drugs, lectins, sugars, nucleic acids (both linear and cyclic polymer configurations), oligosaccharides, proteins, phospholipids and antibodies can all interact with various cell receptors.

Synthetic polymers, such as polyurethanes, polyesters, polycarbonates, polyureas, polyamides, polyethyleneimines, polyarylene sulfides, polysiloxanes, polyimides, and polyacetates can also form an appropriate tag or tag binder. Many other tag/tag binder pairs are also useful in assay systems described herein, as would be apparent to one of skill upon review of this disclosure.

Common linkers such as peptides, polyethers, and the like can also serve as tags, and include polypeptide sequences, such as poly gly sequences of between about 5 and 200 amino acids (SEQ ID NO:526). Such flexible linkers are known to persons of skill in the art. For example, poly(ethylene glycol) linkers are available from Shearwater Polymers, Inc. Huntsville, Alabama. These linkers optionally have amide linkages, sulfhydryl linkages, or heterofunctional linkages.

Tag binders are fixed to solid substrates using any of a variety of methods currently available. Solid substrates are commonly derivatized or functionalized by exposing all or a portion of the substrate to a chemical reagent which fixes a chemical group to the surface which is reactive with a portion of the tag binder. For example, groups which are suitable for attachment to a longer chain portion would include amines, hydroxyl, thiol, and carboxyl groups. Aminoalkylsilanes and hydroxyalkylsilanes can be used to functionalize a variety of surfaces, such as glass surfaces. The construction of such solid phase biopolymer arrays is well described in the literature. *See, e.g.*, Merrifield, *J. Am. Chem. Soc.* 85:2149-2154 (1963) (describing solid phase synthesis of, e.g., peptides); Geysen *et al., J. Immun. Meth.* 102:259-274 (1987) (describing synthesis of solid phase components on pins); Frank & Doring, *Tetrahedron* 44:60316040 (1988) (describing synthesis of various peptide sequences on cellulose disks); Fodor *et al., Science*, 251:767-777 (1991); Sheldon *et al., Clinical Chemistry* 39(4):718-719 (1993); and Kozal *et al., Nature Medicine* 2(7):753759 (1996) (all describing arrays of biopolymers fixed to solid substrates). Non-chemical approaches for fixing tag binders to substrates include other common methods, such as heat, cross-linking by UV radiation, and the like.

AKIVLRRHLSQDHTVPGRPAASELHSRAEHTKENGLPYQSPSVPGSMKLSPQDPRPLSPGALQLAGEKSS
EKGLRERAYGSSGELITSLPISIPLSTVQPNKLPVSIPLASVVLPSRAERARSTPSPVLQPRDPSSTLEK
QIGANAHGAGSRSLALAPAGFSYAGSVAISGALAGSPASLTPGAEPATLDESSSSGSLFATVGSRSSTPQ
HPLLLAQPRNSLPASPAHQLSSSPRLGGAAQGPLPEASKGDLPSDSGFSDPESEAKRRIVFTITTGAGSA
KQSPSSKHSPLTASARGDCVPSHGQDSRRRGRRKRASAGTPSLSAGVSPKRRALPSVAGLFTQPSGSPLN
LNSMVSNINQPLEITAISSPETSLKSSPVPYQDHDQPPVLKKERPLSQTNGAHYSPLTSDEEPGSEDEPS
SARIERKIATISLESKSPPKTLENGGGLAGRKPAPAGEPVNSSKWKSTFSPISDIGLAKSADSPLQASSA
LSQNSLFTFRPALEEPSADAKLAAHPRKGFPGSLSGADGLSPGTNPANGCTFGGGLAADLSLHSFSDGAS
LPHKGPEAAGLSSPLSFPSQRGKEGSDANPFLSKRQLDGLAGLKGEGSRGKEAGEGGLPLCGPTDKTPLL
SGKAAKARDREVDLKNGHNLFISAAAVPPGSLLSGPGLAPAASSAGGAASSAQTHRSFLGPFPPGPQFAL
GPMSLQANLGSVAGSSVLQSLFSSVPAAAGLVHVSSAATRLTNSHAMGSFSGVAGGTVGGVFNHAVPSAS
AHPFGARVGRGAACGSATLGPSPLQAAASASASSFQAPASVETRPPPPPPPPPPLPPPAHLGRSPAGPP
VLHAPPPPNAALPPPPTLLASNPEPALLQSLASLPPNQAFLPPTSAASLPPANASLSIKLTSLPHKGARP
SFTVHHQPLPRLALAQAAPGIPQASATGPSAVWVSLGMPPPYAAHLSGVKPR~~Bottom of Form~~

SEQ ID NO:320

Novel (maps to chromosome 4)

Novel (Chromosome 4)>

GGAATAAAAGAGTGGAAATGGGGATTTCCAGGTGCTCCCCTGGTTCATCTAGGCACCAGAGAGCTGCACTAGCAG
GTCTATCATGAATCTCCTTGGAATGCTCATTTTTAGTCCTACTTGATGTGTCTGTTTCTGGAAATGCAGTATTTT
TAATGTATCTCAACAAAATATTTTATGATTAGTAAGCTTATTCTTATATAAAGGACAATTTTTTTCCTTTTTCAC
AGGTTCTAATAATTTTTTATTTAATAATTAGATCTATTAGATTTTATTCATAACTGTGGTAGTTGAAGTACCTTC
TAAGCTGAGTTCAGATTTGAGAATAAACCTTGGGGTATCATTACAGAAAATTTTGTCTCAATCTGCTTTGTATTT
GAAAGATATGAGATTCTTGAATTATATATCTTACAGACTAGTCCCCAAAAGAATACGTGTTTCCTTACCTTTAAT
TTCTCATGGTAGTTAGTCTGTGAAT

SEQ ID NO:321

Novel peroxidasin-like/ melanoma antigen

>GL2-86-4M13F Direction: sense

CGACCTGGCCAGCCACCGCGGCCTGCTGCGGCAGGGCATCGTGCAGCGGTCCGGGAAGCCGCTGCTCCCCTTCGC
CACCGGGCCGCCCACGGAGTGCATGCGGGACGAGAACGAGAGCCCCATCCCCTGCTTCCTGGCCGGGGACCACCG
CGCCAACGAGCAGCTGGGCCTGACCAGCATGCACACGCTGTGGTTCCGCGAGCACAACCGCATTGCCACGGAGCT
GCTCAAGCTGAACCCGCACTGGGACGGCGACACCATCTACTATGAGACCAGGAAGATCGTGGGTGCGGAGATCCA
GCACATCACCTACCAGCACTGGCTCCCGAAGATCCTGGGGGAGGTGGGCATGAGGACGCTGGGAGAGTACCACGG
CTACGACCCCGGCATCAATGCTGGCATCTTCAACGCCTTCGCCACCGCGGCCTTCAGGTTTGGCCACACGCTTGT
CAACCCACTGCTTTACCGGCTGGACGAGAACTTCCAGCCCATTGCACAAGATCACCTCCCCCTTCACAAAGCTTT
CTTCTCTCCCTTCCGGATTG

SEQ ID NO:322

>GL2_93_2B08_G3F1 Direction: sense

CGACCTGGCCAGCCACCGCGGCCTGCTGCGGCAGGGCATCGTGCAGCGGTCCGGGAAGCCGCTGCTCCCCTTCGC
CACCGGGCCGCCCACGGAGTGCATGCGGGACGAGAACGAGAGCCCCATCCCCTGCTTCCTGGCCGGGGACCACCG
CGCCAACGAGCAGCTGGGCCTGACCAGCATGCACACGCTGTGGTTCCGCGAGCACAACCGCATTGCCACGGAGCT
GCTCAAGCTGAACCCGCACTGGGACGGCGACACCATCTACTATGAGACCAGGAAGATCGTGGGTGCGGAGATCCA
GCACATCACCTACCAGCACTGGCTCCCGAAGATCCTGGGGGAGGTGGGCATGAGGACGCTGGGAGAGTACCACGG
CTACGACCCCGGCATCAATGCTGGCATCTTCAACGCCTTCGCCACCGC

SEQ ID NO:323

Novel peroxidasin-like/ melanoma antigen>

CGACCTGGCCAGCCACCGCGGCCTGCTGCGGCAGGGCATCGTGCAGCGGTCCGGGAAGCCGCTGCTCCCCTTCGC
CACCGGGCCGCCCACGGAGTGCATGCGGGACGAGAACGAGAGCCCCATCCCCTGCTTCCTGGCCGGGGACCACCG
CGCCAACGAGCAGCTGGGCCTGACCAGCATGCACACGCTGTGGTTCCGCGAGCACAACCGCATTGCCACGGAGCT
GCTCAAGCTGAACCCGCACTGGGACGGCGACACCATCTACTATGAGACCAGGAAGATCGTGGGTGCGGAGATCCA
GCACATCACCTACCAGCACTGGCTCCCGAAGATCCTGGGGGAGGTGGGCATGAGGACGCTGGGAGAGTACCACGG
CTACGACCCCGGCATCAATGCTGGCATCTTCAACGCCTTCGCCACCGCGGCCTTCAGGTTTGGCCACACGCTTGT
CAACCCACTGCTTTACCGGCTGGACGAGAACTTCCAGCCCATTGCACAAGATCACCTCCCCCTTCACAAAGCTTT
CTTCTCTCCCTTCCGGATTGTGAATGAGGGCGGCATCGATCCGCTTCTCAGGGGGCTGTTCGGGGTGGCGGGGAA
AATGCGTGTGCCCTCGCAGCTGCTGAACACGGAGCTCACGGAGCGGCTGTTCTCCATGGCACACACGGTGGCTCT
GGACCTGGCGGCCATCAACATCCAGCGGGGCCGGGACCACGGGATCCCACCCTACCACGACTACAGGGTCTACTG
CAATCTATCGGCGGCACACACGTTCGAGGACCTGAAAAATGAGATTAAAAACCCTGAGATCCGG

WHAT IS CLAIMED IS:

1. A method for identifying a compound that modulates angiogenesis, the method comprising the steps of:

(i) contacting the compound with a nucleic acid, or a polypeptide or a fragment thereof encoded by a nucleic acid, wherein the nucleic acid hybridizes under stringent conditions to a second nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:32, SEQ ID NO:43, SEQ ID NO:57, SEQ ID NO:63, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:76, SEQ ID NO:81, SEQ ID NO:86, SEQ ID NO:89, SEQ ID NO:120, SEQ ID NO:128, SEQ ID NO:139, SEQ ID NO:153, SEQ ID NO:163, SEQ ID NO:165, SEQ ID NO:169, SEQ ID NO:171, SEQ ID NO:173, SEQ ID NO:175, SEQ ID NO:183, SEQ ID NO:202, SEQ ID NO:210, SEQ ID NO:218, SEQ ID NO:227, SEQ ID NO:232, SEQ ID NO:248, SEQ ID NO:274, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:297, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:320, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:340, SEQ ID NO:351, SEQ ID NO:365, SEQ ID NO:377, SEQ ID NO:384, SEQ ID NO:406, SEQ ID NO:408, SEQ ID NO:419, SEQ ID NO:421, SEQ ID NO:428, SEQ ID NO:437, SEQ ID NO:439, SEQ ID NO:445, SEQ ID NO:456, SEQ ID NO:462, SEQ ID NO:481, SEQ ID NO:484, SEQ ID NO:493, SEQ ID NO:496, SEQ ID NO:498, SEQ ID NO:519, SEQ ID NO:521, and SEQ ID NO:523 ; and

(ii) determining the functional effect of the compound upon the nucleic acid or polypeptide.

2. The method of claim 1, wherein the functional effect is determined *in vitro*.

3. The method of claim 2, wherein the functional effect is a physical effect.

4. The method of claim 2, wherein the functional effect is determined by measuring ligand or substrate binding to the polypeptide.

5. The method of claim 2, wherein the functional effect is a chemical effect.

ID NO:76, SEQ ID NO:81, SEQ ID NO:86, SEQ ID NO:89, SEQ ID NO:120, SEQ ID NO:128, SEQ ID NO:139, SEQ ID NO:153, SEQ ID NO:163, SEQ ID NO:165, SEQ ID NO:169, SEQ ID NO:171, SEQ ID NO:173, SEQ ID NO:175, SEQ ID NO:183, SEQ ID NO:202, SEQ ID NO:210, SEQ ID NO:218, SEQ ID NO:227, SEQ ID NO:232, SEQ ID NO:248, SEQ ID NO:274, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:297, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:320, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:340, SEQ ID NO:351, SEQ ID NO:365, SEQ ID NO:377, SEQ ID NO:384, SEQ ID NO:406, SEQ ID NO:408, SEQ ID NO:419, SEQ ID NO:421, SEQ ID NO:428, SEQ ID NO:437, SEQ ID NO:439, SEQ ID NO:445, SEQ ID NO:456, SEQ ID NO:462, SEQ ID NO:481, SEQ ID NO:484, SEQ ID NO:493, SEQ ID NO:496, SEQ ID NO:498, SEQ ID NO:519, SEQ ID NO:521, and SEQ ID NO:523.

19. The method of claim 1, wherein the polypeptide comprises a sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:33, SEQ ID NO:44, SEQ ID NO:58, SEQ ID NO:64, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:77, SEQ ID NO:82, SEQ ID NO:87, SEQ ID NO:90, SEQ ID NO:121, SEQ ID NO:129, SEQ ID NO:140, SEQ ID NO:154, SEQ ID NO:164, SEQ ID NO:170, SEQ ID NO:172, SEQ ID NO:174, SEQ ID NO:176, SEQ ID NO:184, SEQ ID NO:203, SEQ ID NO:287, SEQ ID NO:298, SEQ ID NO:309, SEQ ID NO:319, SEQ ID NO:325, SEQ ID NO:331, SEQ ID NO:341, SEQ ID NO:352, SEQ ID NO:366, SEQ ID NO:378, SEQ ID NO:385, SEQ ID NO:407, SEQ ID NO:409, SEQ ID NO:420, SEQ ID NO:429, SEQ ID NO:438, SEQ ID NO:440, SEQ ID NO:446, SEQ ID NO:457, SEQ ID NO:463, SEQ ID NO:482, SEQ ID NO:485, SEQ ID NO:494, SEQ ID NO:497, SEQ ID NO:499, SEQ ID NO:520, SEQ ID NO:522, and SEQ ID NO:524.

20. The method of claim 1, wherein the compound is an antibody.

21. The method of claim 1, wherein the compound is an antisense molecule.

22. The method of claim 1, wherein the compound is a small organic molecule.

23. The method of claim 1, wherein the compound is a peptide.

24. A method for identifying a compound that modulates angiogenesis, the method comprising the steps of:

(i) contacting the compound with a nucleic acid, or a polypeptide or a fragment thereof encoded by a nucleic acid, wherein the nucleic acid hybridizes under stringent conditions to a second nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:32, SEQ ID NO:43, SEQ ID NO:57, SEQ ID NO:63, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:76, SEQ ID NO:81, SEQ ID NO:86, SEQ ID NO:89, SEQ ID NO:120, SEQ ID NO:128, SEQ ID NO:139, SEQ ID NO:153, SEQ ID NO:163, SEQ ID NO:165, SEQ ID NO:169, SEQ ID NO:171, SEQ ID NO:173, SEQ ID NO:175, SEQ ID NO:183, SEQ ID NO:202, SEQ ID NO:210, SEQ ID NO:218, SEQ ID NO:227, SEQ ID NO:232, SEQ ID NO:248, SEQ ID NO:274, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:297, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:320, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:340, SEQ ID NO:351, SEQ ID NO:365, SEQ ID NO:377, SEQ ID NO:384, SEQ ID NO:406, SEQ ID NO:408, SEQ ID NO:419, SEQ ID NO:421, SEQ ID NO:428, SEQ ID NO:437, SEQ ID NO:439, SEQ ID NO:445, SEQ ID NO:456, SEQ ID NO:462, SEQ ID NO:481, SEQ ID NO:484, SEQ ID NO:493, SEQ ID NO:496, SEQ ID NO:498, SEQ ID NO:519, SEQ ID NO:521, and SEQ ID NO:523;

(ii) determining the functional effect of the compound upon the nucleic acid or polypeptide; and

(iii) expressing the nucleic acid or polypeptide in a cell, contacting the nucleic acid or polypeptide with the compound, and determining the phenotypic or chemical effect upon the cell.

25. A method of modulating angiogenesis in a subject, the method comprising the step of administering to the subject a therapeutically effective amount of a compound identified using the method of claim 1.

26. The method of claim 25, wherein the subject is a human.

27. The method of claim 25, wherein the compound is an antibody.

28. The method of claim 25, wherein the compound is an antisense molecule.

NO:320, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:340, SEQ ID NO:351, SEQ ID NO:365, SEQ ID NO:377, SEQ ID NO:384, SEQ ID NO:406, SEQ ID NO:408, SEQ ID NO:419, SEQ ID NO:421, SEQ ID NO:428, SEQ ID NO:437, SEQ ID NO:439, SEQ ID NO:445, SEQ ID NO:456, SEQ ID NO:462, SEQ ID NO:481, SEQ ID NO:484, SEQ ID NO:493, SEQ ID NO:496, SEQ ID NO:498, SEQ ID NO:519, SEQ ID NO:521, and SEQ ID NO:523.

35. An isolated nucleic acid, wherein the nucleic acid acid hybridizes under stringent conditions to a polynucleotide comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:165, SEQ ID NO:202, SEQ ID NO:210, SEQ ID NO:218, SEQ ID NO:227, SEQ ID NO:232, SEQ ID NO:248, SEQ ID NO:274, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:297, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:320, SEQ ID NO:323, SEQ ID NO:324, SEQ ID:329, and SEQ ID:330.

36. The isolated nucleic acid of claim 35, wherein the nucleic acid comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:165, SEQ ID NO:202, SEQ ID NO:210, SEQ ID NO:218, SEQ ID NO:227, SEQ ID NO:232, SEQ ID NO:248, SEQ ID NO:274, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:297, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:320, SEQ ID NO:323, SEQ ID NO:324, SEQ ID:329, and SEQ ID:330.

37. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:287, SEQ ID NO:298, SEQ ID NO:309, SEQ ID NO:319, SEQ ID NO:325, and SEQ ID NO:331.